That which is claimed is:

1. A propagation-defective adenovirus comprising an adenovirus genome comprising one or more deletion(s) in one or more region(s) selected from the group consisting of:
   (a) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region,
   (b) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region, and
   (c) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region.

2. The adenovirus of Claim 1, wherein said adenovirus can be propagated in a cell that transcomplements said deletion(s) in said adenovirus genome.

3. The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell in the absence of a helper.

4. The adenovirus of Claim 1, wherein said adenovirus genome further comprises one or more deletion(s) in the E1 region.

5. The adenovirus of Claim 1, wherein said adenovirus genome further comprises one or more deletion(s) in the E3 region.

6. The adenovirus of Claim 1, wherein said adenovirus genome comprises one or more deletion(s) in the IVa2 region.

7. The adenovirus of Claim 6, wherein said deletion(s) comprises a deletion in the IVa2 region at about nucleotides 4830 to 5766 of the

adenovirus serotype 5 genome or a homologous region of the genome of adenoviruses of other serotypes.

8. The adenovirus of Claim 6, wherein said adenovirus genome further comprises one or more deletion(s) in the polymerase region.

9. The adenovirus of Claim 6, wherein said adenovirus genome further comprises one or more deletion(s) in the E1 region and one or more deletion(s) in the E3 region.

10. The adenovirus of Claim 9, wherein said adenovirus is disclosed herein as [E1$^-$, E3$^-$, IVa2$^-$, pol$^-$]Ad.

11. The adenovirus of Claim 10, wherein said adenovirus comprises one or more heterologous nucleotide sequences.

12. The adenovirus of Claim 1, wherein said adenovirus genome comprises one or more deletion(s) in the 100K region.

13. The adenovirus of Claim 12, wherein said deletion(s) comprises a deletion in the 100K region at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

14. The adenovirus of Claim 12, wherein said adenovirus further comprises one or more deletion(s) in the E1 region.

15. The adenovirus of Claim 14, wherein said adenovirus is disclosed herein as [E1$^-$, 100K$^-$]Ad.

16. The adenovirus of Claim 15, wherein said adenovirus comprises one or more heterologous nucleotide sequences.

17. The adenovirus of Claim 1, wherein said adenovirus genome comprises one or more deletion(s) in the preterminal protein region.

18. The adenovirus of Claim 17, wherein said deletion(s) comprises a deletion in the preterminal protein region at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

19. The adenovirus of Claim 17, wherein said adenovirus genome further comprises one or more deletions in the E1 region.

20. The adenovirus of Claim 17, wherein said adenovirus genome further comprises one or more deletion(s) in the polymerase region.

21. The adenovirus of Claim 20, wherein said deletion(s) in said preterminal protein region comprises a deletion at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes, and said deletion(s) in said polymerase region comprises a deletion at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

22. The adenovirus of Claim 20, wherein said adenovirus further comprises one or more deletions in the E1 region and one or more deletions in the E3 region.

23. The adenovirus of Claim 22, wherein said adenovirus is the adenovirus disclosed herein as [E1-, E3-, pol-, pTP-]Ad.

24. The adenovirus of Claim 23, wherein said adenovirus comprises a one or more heterologous nucleotide sequences.

25. The adenovirus of Claim 1 further comprising one or more heterologous nucleotide sequences.

26. The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) is operatively associated with expression control sequences.

27. The adenovirus of Claim 26, wherein said expression control sequences include a promoter.

28. The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of liver-specific, muscle-specific, and brain-specific promoters.

29. The adenovirus of Claim 27, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1-α promoter, PγK promoter, MFG promoter, and Rous sarcoma virus promoter.

30. The adenovirus of Claim 25, wherein said adenovirus genome further comprises 5' and 3' adenovirus inverted terminal repeat sequences, an adenovirus packaging sequence, and an adenovirus E1A enhancer sequence.

31. The adenovirus of Claim 25, wherein said heterologous nucleotide sequence(s) encodes a protein or peptide.

32. The adenovirus of Claim 31, wherein said protein or peptide is a therapeutic protein or peptide.

33. The adenovirus of Claim 31, wherein said protein or peptide is an immunogenic protein or peptide.

34. The adenovirus of Claim 31, wherein said protein or peptide is a reporter protein or peptide.

35. The adenovirus of Claim 31, wherein said heterologous nucleotide sequence(s) encodes an antisense nucleotide sequence.

36. The adenovirus of Claim 31, wherein said protein or peptide is a lysosomal protein.

37. The adenovirus of Claim 31, wherein said protein or peptide is associated with a metabolic disorder.

38. The adenovirus of Claim 37, wherein said protein or peptide is associated with a lysosomal storage disease.

39. The adenovirus of Claim 38, wherein said protein or peptide is selected from the group consisting of β-galactosidase, β-hexosaminidase A, β-hexosaminidase B, GM_2 activator protein, glucocerebrosidase, arylsulfatase A, galactosylceramidase, acid sphingomyelinase, acid ceramidase, acid lipase, α-L-iduronidase, iduronate sulfatase, heparan N-sulfatase, α-N-acetylglucosaminidase acetyl-CoA, glucosaminide acetyltransferase, N-acetylglucosamine-6-sulfatase, arylsulfatase B, β-glucuronidase, α-mannosidase, β-mannosidase, α-L-fucosidase, N-aspartyl-β-glucosaminidase, α-neuraminidase, lysosomal protective protein, α-N-acetyl-galactosaminidase, N-acetylglucosamine-1-phosphotransferase, cystine transport protein, sialic acid transport protein, the CLN3 gene product, palmitoyl-protein thioesterase, saposin A, saposin B, saposin C, and saposin D.

40. The adenovirus of Claim 37, wherein said protein or peptide is associated with a glycogen storage disease.

41. The adenovirus of Claim 40, wherein said protein or peptide is selected from the group consisting of glucose 6-phosphatase, lysosomal acid α glucosidase, glycogen debranching enzyme, branching enzyme, muscle phosphorylase, liver phosphorylase, phosphorylase kinase, muscle phosphofructokinase, glycogen synthase, phosphoglucoisomerase, muscle phosphoglycerate kinase, phosphoglycerate mutase, and lactate dehydrogenase.

42. The adenovirus of Claim 41, wherein said protein or peptide is lysosomal acid α-glucosidase.

43. The adenovirus of Claim 42, wherein said protein or peptide is human lysosomal acid α-glucosidase.

44. A propagation-defective adenovirus comprising an adenovirus genome comprising:

(a) one or more deletions in the E1 region, wherein said deletion(s) essentially prevents the expression of one or more functional E1 proteins from said deleted region, and

(b) one or more deletions in the polymerase region, wherein said deletion(s) essentially prevents the expression of a functional polymerase protein from said deleted region.

45. The adenovirus of Claim 44, wherein said adenovirus can be propagated in a cell that transcomplements said deletions in said adenovirus genome.

46. The adenovirus of Claim 1, wherein said adenovirus can be propagated in a transcomplementing cell in the absence of a helper.

47. The adenovirus of Claim 44, wherein said adenovirus genome further comprises one or more deletions in the E3 region.

48. The adenovirus of Claim 47, wherein said adenovirus is the adenovirus disclosed herein as [E1-, E3-, pol-]Ad.

49. The adenovirus of Claim 48, wherein said adenovirus comprises one or more heterologous nucleotide sequences.

50. The adenovirus of Claim 44, wherein said adenovirus genome further comprises one or more deletions in the 100K region.

51. The adenovirus of Claim 44, wherein said adenovirus further comprises one or more deletions in the IVa2 region.

52. The adenovirus of Claim 44, wherein said adenovirus genome further comprises one or more deletions in the preterminal protein region.

53. The adenovirus of Claim 52, wherein said adenovirus genome further comprises one or more deletions in the E3 region and one or more deletions in the IVa2 region.

54. The adenovirus of Claim 52, wherein said adenovirus genome further comprises one or more deletions in the E3 region and one or more deletions in the 100K region.

55. The adenovirus of Claim 52, wherein said adenovirus genome further comprises one or more deletions in the E3 region, one or more deletions in the IVa2 region, and one or more deletions in the 100K region.

56. The adenovirus of Claim 44, wherein said adenovirus genome further comprises a deletion in the adenovirus polymerase region at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

57. The adenovirus of Claim 44, wherein said adenovirus further comprises one or more heterologous nucleotide sequences.

58. The adenovirus of Claim 57, wherein said adenovirus is disclosed herein as AdLacZΔpol or AdLacZΔpp.

59. A propagation-defective adenovirus comprising an adenovirus genome comprising a heterologous nucleotide sequence encoding a lysosomal acid α-glucosidase and one or more deletions in one or more regions selected from the group consisting of:

(a) the polymerase region, wherein said deletion(s) essentially prevents the expression of a functional polymerase from said deleted region,

(b) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region,

(c) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region; and

(d) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region.

60. The adenovirus of Claim 59, wherein said adenovirus genome comprises a deletion in the polymerase region at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

61. The adenovirus of Claim 59, wherein said adenovirus comprises a deletion in the preterminal protein region at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

62. The adenovirus of Claim 59, wherein said adenovirus genome comprises one or more deletions in the polymerase region and one or more deletions in the preterminal protein region.

63. The adenovirus of Claim 59, wherein said heterologous nucleotide sequence is operatively associated with a promoter.

64. The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of liver-specific and muscle-specific promoters.

65. The adenovirus of Claim 63, wherein said promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1-α promoter, PγK promoter, MFG promoter, and Rous sarcoma virus promoter.

66. The adenovirus of Claim 59, wherein said adenovirus is selected from the group consisting of AdhGAAΔpol, Ad/EF1-α/hGAAΔpol, Adh5'sGAAΔpol, Ad/EF1-α/h5'sGAAΔpol, AdhGAAΔpp, Ad/EF1-α/hGAAΔpp, Adh5'sGAAΔpp, Ad/EF1-α/h5'sGAAΔpp.

67. The adenovirus of Claim 59, wherein said adenovirus genome comprises a deletion in the 100K region at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

68. The adenovirus of Claim 59, wherein said adenovirus genome comprises a deletion in the adenovirus IVa2 region at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a corresponding region of adenoviruses of other serotypes.

69. A cell comprising the adenovirus of Claim 1.

70. The cell of Claim 69, wherein said adenovirus comprises one or more heterologous nucleotide sequences encoding a protein or peptide.

71. The cell of Claim 69, wherein said cell is a mammalian cell.

72. A cell comprising the adenovirus of Claim 44.

73. The cell of Claim 72, wherein said adenovirus comprises one or more heterologous nucleotide sequences encoding a protein or peptide.

74. The cell of Claim 72, wherein said cell is a mammalian cell.

75. A cell comprising the adenovirus of Claim 59.

76. The cell of Claim 75, wherein said adenovirus comprises one or more heterologous nucleotide sequences encoding a protein or peptide.

77. The cell of Claim 75, wherein said cell is a mammalian cell.

78. A cell comprising an isolated DNA comprising a nucleotide sequence encoding an adenovirus 100K protein.

79. The cell of Claim 78, wherein said cell is a mammalian cell.

80. The cell of Claim 78, wherein said cell can propagate an adenovirus genome that essentially lacks expression of a functional 100K protein.

81. The cell of Claim 78, wherein said nucleotide sequence is stably integrated into the genome of the packaging cell.

82. The cell of Claim 81, wherein said cell is a K-16 cell.

83. The cell of Claim 78, wherein said nucleotide sequence further encodes a constitutive promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.

84. The cell of Claim 83, wherein said cell is a C7 cell constitutively expressing the 100K protein.

85. The cell of Claim 78, wherein said nucleotide sequence encodes an inducible promoter that is operatively associated with the sequence encoding said adenovirus 100K protein.

86. The cell of Claim 78, further comprising an adenovirus genome, wherein said adenovirus genome comprises one or more deletion(s) in the 100K region, and further wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said 100K region.

87. A cell comprising an isolated DNA comprising a nucleotide sequence encoding an adenovirus IVa2 protein.

88. The cell of Claim 87, wherein said cell is a mammalian cell.

89. The cell of Claim 87, wherein said cell can propagate an adenovirus genome that essentially lacks expression of a functional IVa2 protein.

90. The cell of Claim 87, wherein said nucleotide sequence is stably integrated into the genome of the packaging cell.

91. The cell of Claim 90, wherein said cell is a B6 cell or a C7 cell.

92. The cell of Claim 87, wherein said nucleotide sequence encodes a constitutive promoter that is operatively associated with the sequence encoding said adenovirus IVa2 protein.

93. An isolated DNA comprising a nucleotide sequence encoding an adenovirus 100K protein, wherein there is one or more deletion(s) in the nucleotide sequence encoding said adenovirus 100K protein.

94. An isolated DNA of Claim 93, wherein said isolated DNA comprises an adenovirus genome comprising the nucleotide sequence encoding the deleted adenovirus 100K protein.

95. The isolated DNA of Claim 94, wherein said deletion(s) in the 100K region comprises a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

96. A vector comprising the isolated DNA of Claim 94.

97. The vector of Claim 96, wherein said vector is a plasmid.

98. The vector of Claim 97, wherein said vector is disclosed herein as pcDNA3+100K.

99. An isolated DNA comprising a nucleotide sequence encoding an adenovirus IVa2 protein, wherein there one or more deletion(s) in the nucleotide sequence encoding said adenovirus IVa2 protein.

100. An isolated DNA of Claim 99, wherein said isolated DNA comprises an adenovirus genome comprising the nucleotide sequence encoding the deleted adenovirus IVa2 region.

101. The isolated DNA of Claim 100, wherein said deletion(s) in the IVa2 region comprises a deletion at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

102. A vector comprising the isolated DNA of Claim 99.

103. The vector of Claim 102, wherein said vector is a plasmid.

104. The vector of Claim 103, wherein said plasmid is selected from the group consisting of:

(a) pAdAscLΔIVa2

(b) pAdAscLΔIVa2, Δpol

(c) pAdAscLIVa2, Δpp(1.6); and

(d) pAdAscLΔIVa2, Δpp (2.4).

105. A method of producing a propagation-defective adenovirus particle comprising one or more deletion(s) in the adenovirus genome, comprising:

introducing an adenovirus into a mammalian cell, wherein the introduced adenovirus comprises an adenovirus genome comprising one or more deletions in one or more regions selected from the group consisting of:

(a) the 100K region, wherein the deletion(s) essentially prevents the expression of a functional 100K protein from the deleted region,

(b) the IVa2 region, wherein the deletion(s) essentially prevents the expression of a functional IVa2 protein from the deleted region, and

(c) and the preterminal protein region, wherein the deletion(s) essentially prevents the expression of a functional preterminal protein from the deleted region;

wherein the mammalian cell transcomplements the function(s) deleted from the adenovirus genome; and

collecting the propagation-defective adenovirus particle.

106. The method of Claim 105, wherein the collected adenovirus has a titer of at least 100 infectious units per cell.

107. The method of Claim 105, wherein the adenovirus genome further comprises one or more deletion(s) in the E1 region and the mammalian cell further transcomplements the deletion(s).

108. The method of Claim 105, wherein the adenovirus genome further comprises one or more deletion(s) in the E3 region.

109. The method of Claim 105, wherein the adenovirus genome further comprises one or more deletion(s) in the polymerase region and the mammalian cell further transcomplements the deletion.

110. The method of Claim 105, wherein the adenovirus genome comprises one or more deletion(s) in the adenovirus 100K region.

111. The method of Claim 110, wherein the deletion(s) in the 100K region comprises a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

112. The method of Claim 111, wherein the introduced adenovirus is disclosed herein as [$E1^-$, $100K^-$]Ad.

113. The method of Claim 110, wherein the mammalian cell comprises a nucleotide sequence encoding a functional 100K protein stably integrated into the genome of the mammalian cell.

114. The method of Claim 113, wherein the mammalian cell is a K-16 cell.

115. The method of Claim 110, wherein the mammalian cell constitutively expresses the functional 100K protein.

116. The method of Claim 115, wherein the mammalian cell is a C7 cell constitutively expressing the 100K protein.

117. The method of Claim 105, wherein the adenovirus genome comprises one or more deletion(s) in the adenovirus IVa2 region.

118. The method of Claim 117, wherein the deletion(s) comprise a deletion in the IVa2 region at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

119. The method of Claim 117, wherein the adenovirus genome further comprises one or more deletion(s) in the polymerase region and the mammalian cell further transcomplements the deletion.

120. The method of Claim 119, wherein the adenovirus genome further comprises one or more deletion(s) in the E1 region and one or more deletion(s) in the E3 region and the mammalian cell further transcomplements the E1 deletion.

121. The method of Claim 120, wherein the adenovirus is disclosed herein as [$E1^-$, $E3^-$, $IVa2^-$, pol^-]Ad.

122. The method of Claim 117, wherein the mammalian cell comprises a nucleotide sequence encoding a functional IVa2 protein stably integrated into the genome of the mammalian cell.

123. The method of Claim 122, wherein the mammalian cell is a B6 cell or a C7 cell.

124. The method of Claim 122, wherein the mammalian cell constitutively expresses the functional IVa2 protein.

125. The method of Claim 105, wherein the adenovirus comprises one or more deletion(s) in the adenovirus preterminal protein region.

126. The method of Claim 125, wherein the deletion(s) in the preterminal protein region comprises a deletion at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

127. The method of Claim 125, wherein the introduced adenovirus is disclosed herein as [E1-, E3-, pol-, pTP-]Ad.

128. The method of Claim 125, wherein the mammalian cell comprises a nucleotide sequence encoding a functional preterminal protein stably integrated into the genome of the mammalian cell.

129. The method of Claim 128, wherein the mammalian cell is a C7 cell.

130. The method of Claim 125, wherein the mammalian cell constitutively expresses a functional preterminal protein.

131. The method of Claim 125, wherein the adenovirus genome further comprises one or more deletion(s) in the polymerase region and the mammalian cell further transcomplements the deletion.

132. The method of Claim 105, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.

133. A propagation-defective adenovirus particle produced by the method of Claim 105.

134. A method of producing a propagation-defective adenovirus particle comprising one or more deletions in the polymerase region and one or more deletions in the E1 region, comprising:

introducing an adenovirus into a mammalian cell, wherein the introduced adenovirus comprises an adenovirus genome comprising:

(a) one or more deletions in the polymerase region, wherein the deletion(s) essentially prevents the expression of a functional polymerase from the deleted region,

(b) one or more deletions in the E1 region, wherein the deletion(s) essentially prevents the expression of one or more functional E1 proteins from said deleted region, and

further wherein the mammalian cell transcomplements the deleted functions in the adenovirus genome; and

collecting the propagation-defective adenovirus particle.

135. The method of Claim 134, wherein the collected adenovirus has a titer of at least 100 infectious units per cell.

136. The method of Claim 134, wherein the deletion(s) in the polymerase region comprises a deletion at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

137. The method of Claim 134, wherein the adenovirus is disclosed herein as [E1-, E3-, pol-]Ad.

138. The method of Claim 134, wherein a nucleotide sequence encoding a functional polymerase protein is stably integrated into the genome of the mammalian cell.

139. The method of Claim 138, wherein the mammalian cell is a B6 or C7 cell.

140. The method of Claim 134, wherein the mammalian cell constitutively expresses a functional polymerase protein.

141. The method of Claim 134, wherein the adenovirus further comprises one or more deletion(s) in the adenovirus E3 region.

142. The method of Claim 134, wherein the introduced adenovirus further comprises one or more deletion(s) in the preterminal protein region, and wherein the mammalian cell transcomplements the deleted preterminal protein functions in the adenovirus genome.

143. The method of Claim 134, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.

144. The method of Claim 143, wherein the introduced adenovirus is selected from the group consisting of AdhGAAΔpol, Ad/EF1-α/hGAAΔpol, Adh5'sGAAΔpol, Ad/EF1-α/h5'sGAAΔpol, AdhGAAΔpp, Ad/EF1-α/hGAAΔpp, Adh5'sGAAΔpp, Ad/EF1-α/h5'sGAAΔpp.

145. A propagation-defective adenovirus particle produced by the method of Claim 134.

146. A method of producing a propagation-defective adenovirus particle, comprising:

introducing a bacterial plasmid comprising an adenovirus genome into a bacterial cell, wherein said adenovirus genome comprises one or more deletions in one or more regions selected from the group consisting of:

(a) the polymerase region, wherein said deletion(s) essentially prevents the expression of a functional polymerase from said deleted region,

(b) the preterminal protein region, wherein said deletion(s) essentially prevents the expression of a functional preterminal protein from said deleted region,

(c) the 100K region, wherein said deletion(s) essentially prevents the expression of a functional 100K protein from said deleted region, and

(d) the IVa2 region, wherein said deletion(s) essentially prevents the expression of a functional IVa2 protein from said deleted region;

amplifying the bacterial plasmid in the bacterial cell;

recovering the amplified bacterial plasmid from the bacterial cell;

linearizing the recovered bacterial plasmid;

introducing the linearized plasmid into a mammalian cell that transcomplements the deleted functions in the adenovirus genome; and

collecting the propagation-defective adenovirus particle.

147. The method of Claim 146, wherein the adenovirus genome further comprises one or more heterologous nucleotide sequences.

148. The method of Claim 147, wherein the heterologous nucleotide sequence(s) encodes a lysosomal acid α-glucosidase.

149. A method of delivering a nucleotide sequence into a cell, comprising introducing into a cell a propagation-defective adenovirus comprising an adenovirus genome comprising a heterologous nucleotide sequence and one or more deletions in one or more regions selected from the group consisting of:

(a) the 100K region, wherein the deletion(s) essentially prevents the expression of a functional 100K protein from the deleted region,

(b) the IVa2 region, wherein the deletion(s) essentially prevents the expression of a functional IVa2 protein from the deleted region, and

(c) the preterminal protein region, wherein the deletion(s) essentially prevents the expression of a functional preterminal protein from the deleted region.

150. The method of Claim 149, wherein at least about 10,000 infectious units of the adenovirus are administered to the cell.

151. The method of Claim 149, wherein the adenovirus genome further comprises one or more deletions in the polymerase region.

152. The method of Claim 149, wherein the adenovirus genome comprises two heterologous nucleotide sequences.

153. The method of Claim 149, wherein the nucleotide sequence encodes a protein or peptide.

154. The method of Claim 153, wherein the nucleotide sequence encodes a therapeutic protein or peptide.

155. The method of Claim 153, wherein the nucleotide sequence encodes an immunogenic protein or peptide.

156. The method of Claim 153, wherein said protein or peptide is a lysosomal protein.

157. The method of Claim 153, wherein said protein or peptide is associated with a metabolic disorder.

158. The method of Claim 157, wherein said protein or peptide is associated with a lysosomal storage disease.

159. The method of Claim 157, wherein said protein or peptide is associated with a glycogen storage disease.

160. The method of Claim 159, wherein said protein or peptide is selected from the group consisting of glucose 6-phosphatase, lysosomal acid α glucosidase, glycogen debranching enzyme, branching enzyme, muscle phosphorylase, liver phosphorylase, phosphorylase kinase, muscle phosphofructokinase, glycogen synthase,

phosphoglucoisomerase, muscle phosphoglycerate kinase, phosphoglycerate mutase, and lactate dehydrogenase.

161. The method of Claim 160, wherein said protein or peptide is a human lysosomal acid α-glucosidase.

162. The method of Claim 149, wherein the cell is selected from the group consisting of a neuronal cell, a retinal cell, an epithelial cell, a muscle cell, a pancreatic cell, a hepatic cell, a fibroblast, an endothelial cell, a germ cell, a lung cell, and a prostate cell.

163. The method of Claim 149, wherein the heterologous nucleotide sequence is operatively associated with expression control sequences.

164. The method of Claim 163, wherein the heterologous nucleotide sequence is operatively associated with a promoter.

165. The method of Claim 164, wherein the promoter is selected from the group consisting of liver-specific, muscle-specific, and brain specific promoters.

166. The method of Claim 164, wherein the promoter is selected from the group consisting of the CMV promoter, albumin promoter, EF1-α promoter, PγK promoter, MFG promoter, and Rous sarcoma virus promoter.

167. The method of Claim 149, wherein the adenovirus genome comprises one or more deletions in the 100K region.

168. The method of Claim 167, wherein the deletion(s) in the 100K region comprises a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a homologous region of adenoviruses of other serotypes.

169. The method of Claim 167, wherein the adenovirus is disclosed herein as [E1$^-$, 100K$^-$]Ad.

170. The method of Claim 149, wherein the adenovirus genome comprises one or more deletions in the adenovirus IVa2 region.

171. The method of Claim 170, wherein the deletion(s) in the IVa2 region comprise a deletion at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or a homologous region adenoviruses of other serotypes.

172. The method of Claim 170, wherein the adenovirus is disclosed herein as [E1$^-$, E3$^-$, IVa2$^-$, pol$^-$]Ad.

173. The method of Claim 149, wherein the adenovirus genome comprises one or more deletions in the preterminal protein region.

174. The method of Claim 173, wherein the deletion(s)in the preterminal protein region comprise a deletion at about nucleotides 9198 to 9630 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

175. The method of Claim 149, wherein the adenovirus genome further comprises one or more deletions in the adenovirus polymerase region.

176. The method of Claim 175, wherein the deletion(s) in the polymerase region comprise a deletion at about nucleotides 7274 to 7881 of the adenovirus serotype 5 genome or a corresponding region of the genome of adenoviruses of other serotypes.

177. A method of administering a nucleotide sequence to a subject, comprising administering to a subject a biologically-effective amount of a propagation-defective adenovirus particle comprising an adenovirus

genome comprising a heterologous nucleotide sequence and one or more deletions in one or more regions selected from the group consisting of:

(a) the 100K region, wherein the deletion(s) essentially prevents the expression of a functional 100K protein from the deleted region,

(b) the IVa2 region, wherein the deletion(s) essentially prevents the expression of a functional IVa2 protein from the deleted region, and

(c) the preterminal protein region, wherein the deletion(s) essentially prevents the expression of a functional preterminal protein from the deleted region.

178. The method of Claim 177, wherein the adenovirus genome further comprises one or more deletions in the polymerase region.

179. The method of Claim 177, wherein at least about 10,000 infectious units of the adenovirus are administered to the subject.

180. The method of Claim 179, wherein the heterologous nucleotide sequence encodes a peptide or protein.

181. The method of Claim 180, wherein the protein or peptide is a lysosomal acid α-glucosidase.

182. The method of Claim 177, wherein the subject is selected from the group consisting of avian subjects and mammalian subjects.

183. The method of Claim 182, wherein the subject is a human subject.

184. The method of Claim 183, wherein the human subject has been diagnosed with lysosomal acid α-glucosidase deficiency.

185. The method of Claim 184, wherein the human subject has been diagnosed with lysosomal acid α-glucosidase deficiency.

186. The method of Claim 177, wherein the adenovirus is administered by a route selected from the group consisting of oral, rectal, transmucosal, transdermal, inhalation, intravenous, subcutaneous, intradermal, intramuscular, and intraarticular administration.

187. The method of Claim 177, wherein the adenovirus is delivered to the liver by a method selected from the group consisting of intravenous administration, intraportal administration, intrabiliary administration, intra-arterial administration, and direct injection into the liver parenchyma.

188. A method of delivering a nucleotide sequence into a cell, comprising introducing into a cell a propagation-defective adenovirus comprising an adenovirus genome comprising a heterologous nucleotide sequence and

(a) one or more deletions in the E1 region, wherein the deletion(s) essentially prevents the expression of one or more functional E1 proteins from the deleted region, and

(b) one or more deletions in the polymerase region, wherein the deletion(s) essentially prevents the expression of a functional polymerase from the deleted region.

189. The method of Claim 188, wherein at least about 10,000 infectious units of the adenovirus are administered to the cell.

190. A method of administering a nucleotide sequence to a subject, comprising administering to a subject a biologically-effective amount of a propagation-defective adenovirus comprising an adenovirus genome comprising a heterologous nucleotide sequence and

(a) one or more deletions in the E1 region, wherein the deletion(s) essentially prevents the expression of one or more functional E1 proteins from the deleted region, and

(b) one or more deletions in the polymerase region, wherein the deletion(s) essentially prevents the expression of a functional polymerase from the deleted region.

191. The method of Claim 190, wherein at least about 10,000 infectious units of the adenovirus are administered to the subject.

192. A method of treating a subject with a lysosomal acid α-glucosidase deficiency comprising administering a biologically-effective amount of a nucleotide sequence encoding a lysosomal acid α-glucosidase to the liver of the subject.

193. The method of Claim 192, wherein the liver expresses and secretes the encoded lysosomal acid α-glucosidase, which is transported to a muscle-tissue in a therapeutically-effective amount.

194. The method of Claim 192, wherein an adenovirus vector comprising the nucleotide sequence encoding the lysosomal acid α-glucosidase is administered to the subject.

195. The method of Claim 194, wherein the nucleotide sequence encodes an lysosomal acid α-glucosidase precursor protein.

196. The method of Claim 194, wherein the adenovirus vector is selected from the group consisting of AdhGAAΔpol, Ad/EF1-α/hGAAΔpol, Adh5'sGAAΔpol, Ad/EF1-α/h5'sGAAΔpol, AdhGAAΔpp, Ad/EF1-α/hGAAΔpp, Adh5'sGAAΔpp, Ad/EF1-α/h5'sGAAΔpp.

197. The method of Claim 192, wherein the nucleotide sequence is administered to the liver by a method selected from the group

consisting of intravenous administration, intraportal administration, intrabiliary administration, intra-arterial administration, and direct injection into the liver parenchyma.

198. The method of Claim 192, wherein the subject is a mammalian subject.

199. The method of Claim 198, wherein the subject is a human subject.

200. A method of treating a subject with lysosomal acid α-glucosidase deficiency, comprising administering to the subject a therapeutically-effective amount of a propagation-defective adenovirus comprising an adenovirus genome comprising a heterologous nucleotide sequence that encodes a lysosomal acid α-glucosidase and one or more deletions in one or more regions selected from the group consisting of:

(a) the 100K region, wherein the deletion(s) essentially prevents the expression of a functional 100K protein from the deleted region,

(b) the IVa2 region, wherein the deletion(s) essentially prevents the expression of a functional IVa2 protein from the deleted region,

(c) the preterminal protein region, wherein the deletion(s) essentially prevents the expression of a functional preterminal protein from the deleted region, and

(d) adenovirus polymerase region, wherein the deletion(s) essentially prevents the expression of a functional polymerase protein from the adenovirus genome.

201. The method of Claim 200, wherein the adenovirus is selected from the group consisting of AdhGAAΔpol, Ad/EF1-α/hGAAΔpol, Adh5'sGAAΔpol, Ad/EF1-α/h5'sGAAΔpol, AdhGAAΔpp, Ad/EF1-α/hGAAΔpp, Adh5'sGAAΔpp, Ad/EF1-α/h5'sGAAΔpp.

202. The method of Claim 200, wherein the lysosomal acid α-glucosidase is a human lysosomal acid α-glucosidase.

203. The method of Claim 200, wherein the subject is selected from the group consisting of avian subjects and mammalian subjects.

204. The method of Claim 203, wherein the subject is a human subject.

205. The method of Claim 200, wherein the adenovirus is administered by a method selected from the group consisting of oral, rectal, transmucosal, transdermal, inhalation, intravenous, subcutaneous, intradermal, intramuscular, and intraarticular administration.

206. The method of Claim 200, wherein the adenovirus is delivered to the liver by a method selected from the group consisting of intravenous administration, intraportal administration, intrabiliary administration, intra-arterial administration, and direct injection into the liver parenchyma.

207. A method of producing a gutted adenovirus containing a minichromosome, comprising:

introducing into a mammalian cell expressing a functional 100K protein:

a plasmid comprising an adenovirus inverted terminal repeat (ITR), an adenovirus packaging sequence, and a heterologous nucleotide sequence, and

a helper adenovirus comprising an adenovirus genome comprising one or more deletions in the adenovirus 100K region, wherein the deletion(s) prevents the expression of a functional protein from the deleted region;

collecting the gutted adenovirus containing the minichromosome from the mammalian cell.

208. The method of Claim 207, wherein the deletion(s) in the 100K region comprises a deletion at about nucleotides 24,990 to 25,687 of the adenovirus serotype 5 genome or a homologous region adenoviruses of other serotypes.

209. The method of Claim 207, wherein the introduced helper adenovirus is disclosed herein as [E1$^-$, 100K$^-$]Ad.

210. The method of Claim 207, wherein the adenovirus genome further comprises one or more deletions in the IVa2 region and the mammalian cell expresses a functional IVa2 protein.

211. The method of Claim 207, wherein the adenovirus genome further comprises one or more deletions in the polymerase region and the mammalian cell expresses a functional polymerase protein.

212. The method of Claim 207, wherein the adenovirus genome further comprises one or more deletions in the preterminal protein region and the mammalian cell expresses a functional preterminal protein.

213. The method of Claim 207, wherein the nucleotide sequence encoding the functional 100K protein is stably integrated into the genome of the mammalian cell.

214. The method of Claim 213, wherein the mammalian cell is a K-16 cell.

215. The method of Claim 207, wherein the mammalian cell constitutively expresses the functional 100K protein.

216. The method of Claim 215, wherein said mammalian cell is a C7 cell constitutively expressing the 100K protein.

217. The method of Claim 207, wherein the helper adenovirus lacks a packaging sequence.

218. The method of Claim 207, wherein the helper adenovirus has a modified packaging signal that does not promote the encapsidation of the helper plasmid.

219. The method of Claim 207, wherein the helper adenovirus further comprises lox sites flanking the packaging sequence and the mammalian cell produces the cre recombinanse protein.

220. A method of delivering a nucleotide sequence into a cell comprising introducing into the cell a composition comprising a plurality of the gutted adenovirus particles of Claim 207.

221. The method of Claim 220, wherein said introducing is carried out *in vivo*.

222. The method of Claim 207, further comprising the step of separating the gutted adenovirus from contaminating helper adenovirus.

223. A method of producing a gutted adenovirus containing a minichromosome, comprising:
introducing into a mammalian cell expressing a functional IVa2 protein:
a plasmid comprising an adenovirus inverted terminal repeat (ITR), an adenovirus packaging sequence, and a heterologous nucleotide sequence, and
a helper adenovirus comprising an adenovirus genome comprising at one or more deletions in the adenovirus IVa2 region, wherein the deletion(s) prevents the expression of a functional protein,
collecting the gutted adenovirus containing the minichromosome from the mammalian cell.

224. The method of Claim 223, wherein the deletion is at about nucleotides 4830 to 5766 of the adenovirus serotype 5 genome or the corresponding region of the genome of adenoviruses of other serotypes.

225. The method of Claim 223, wherein the adenovirus genome further comprises one or more deletions in the adenovirus polymerase region and the mammalian cell expresses a functional polymerase protein.

226. The method of Claim 223, wherein the adenovirus genome further comprises one or more deletions in the preterminal protein region and the mammalian cell expresses a functional preterminal protein.

227. The method of Claim 223, wherein the nucleotide sequence encoding the functional IVa2 protein is stably integrated into the genome of the mammalian cell.

228. The adenovirus of Claim 227, wherein said adenovirus is disclosed herein as [E1-, E3-, IV a2-, pol-]Ad.

229. The method of Claim 227, wherein the mammalian cell is a C7 cell.

230. The method of Claim 223, wherein the mammalian cell constitutively expresses the functional IVa2 protein.

231. The method of Claim 223, wherein the helper adenovirus lacks a packaging sequence.

232. The method of Claim 223, wherein the helper adenovirus has a modified packaging signal that does not promote the encapsidation of the helper plasmid.

233. The method of Claim 223, wherein the helper adenovirus further comprises lox sites flanking the packaging sequence and the mammalian cell produces the cre recombinase protein.

234. A method of delivering a nucleotide sequence into a cell comprising introducing into the cell the gutted adenovirus containing an adenovirus minichromosome of Claim 223.

235. The method of Claim 334, wherein said introducing is carried out *in vivo*.

236. The method of Claim 334, further comprising the step of separating the gutted adenovirus from contaminating helper adenovirus.